DETAILED ACTION

1. Claims 1-16 are currently pending.

Election/Restrictions

2. Applicant's election without traverse of Group I (claims 1-15), SEQ ID NO: 2 of WO97/09425 (as SEQ ID NO: 11 of the present application) and hypertension in Response to Election / Restriction, filed 03/03/2008, is acknowledged.

Claims 6-10 and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention/species, there being no allowable generic or linking claim.

Claims 1-5 and 11-15 are currently under examination as they read on a method for treating or preventing congestive heart failure comprising administering a polypeptide wherein the polypeptide reads on the elected species of SEQ ID NO: 2 of WO97/0925 (as SEQ ID NO: 11 of the present application).

Priority

3. The domestic priority date for claims 1-5 and 11-15 is deemed the effective filing date of USSN 09/298,121, i.e., 04/23/1999.

Applicant is invited to amend the first line of the specification to update the status of priority application USSN 09/298,121, now U.S Patent 6,635,249.

Specification

4. Applicant is requested to review the application for spelling error, the use of trademarks, embedded hyperlinks and/or other form of browser-executable code.

Trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Embedded hyperlinks and/or other form of browser-executable code are impermissible in the text of the application as they represent an improper incorporation by reference.

Claim Objections

5. Claim 2 is objected to because of the following informalities:

Applicant is invited to amend the claims to recited the elected species of "SEQ ID NO: 11" in place of "SEQ ID NO: 2 of WO97/09425".

Appropriate correction is required.

Claim Rejections - 35 USC § 112 first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-5 and 11-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the **enablement** requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following grounds of enablement rejection pertain to ***preventing*** *congestive heart failure:*

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of *Ex parte Aggarwal*, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

The specification does not adequately teach how to effectively prevent any disease in mammals by administering a polypeptide of SEQ ID NO: 11 of the present invention. The specification does not teach how to extrapolate data obtained from various in vitro or in vivo observations with the pharmaceutical composition comprising the antibody to the development of effective preventing human diseases such congestive heart failure encompassed by the claimed invention and consistent with the disclosure of various diseases and disorders disclosed on page 12 of the instant specification.

According to *The Merck Manual of Diagnosis and Therapy*, the etiology of congestive heart failure involve multitudes of factors that can impair cardiac performance and produce HF such as cardiac factors including myocardial damage (e.g., acute in MI or myocarditis, chronic in fibrosis due to various disorders), valvular disorders, arrhythmias (tachyarrhythmias or bradyarrhythmias), and reduced substrate availability (i.e., ischemia) and systemic factors including any disorder that increases demand for CO (causing high-output HF) or resistance to output (afterload), such as systemic hypertension (see *The Merck Manuals Online Medical Library,* [online]. Whitehouse Station, NJ: Merck Research Laboratories, 2006-2007. [retrieved on 06/16/2008]. Retrieved from the Internet: < URL:

http://www.merck.com/mmpe/print/sec07/ch074/ch074b.html >. Heart Failure, pages 1-15, see pages 4-5). However, the instant disclosure does not provide sufficient in vitro or in vivo evidence showing that the administration of a polypeptide comprising an EFG-like domain such as SEQ ID NO: 11 can counter-act the cause or the manifestation of congestive heart failure as defined by *The Merck Manual of Diagnosis and Therapy* in order to prevent the disease.

Furthermore, it is noted that, under the broadest reasonable interpretation, a method for preventing congestive heart failure broadly encompasses a target population of those who do not necessarily have congestive heart failure. Therefore, one of skill in the art would not know how to practice the claimed invention without undue amount of experimentation because one of skill in the art would not know who appropriate patient population to which target the claimed invention.

Also, it is noted that experimental protocols usually are conducted under defined conditions wherein the antagonist and the stimulus / insult occur at the same or nearly the same time. Receptor targeting is much easier to achieve under such controlled conditions than that experienced in the human disorders or diseases such as congestive heart failure targeted by the claimed invention.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective methods to prevent congestive heart failure and in view of lack of sufficient working examples provided by Applicant of using the polypeptide, undue experimentation would be required to practice the claimed methods of preventing diseases with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for preventing the diseases or disorders encompassed by the claimed methods.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicant is invited to amend the claims to avoid the recitation of "preventing" to obviate this rejection.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571)272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen, Ph.D./
Examiner, Art Unit 1644
June 18, 2008

/Phillip Gambel/
Phillip Gambel, Ph.D., J.D.
Primary Examiner
Art Unit 1644
Technology Center 1600
June 18, 2008